REMARKS

Claims 23-50 and 68-87 are pending in the present application. Claims 23, 68 and 80 are independent claims.

The present invention relates to a method of determining a glucose concentration in a body fluid using a glucose-containing perfusate.

The title of the application is objected to as not aptly descriptive. The title is amended to remove the phrase "and arrangement" and to add the phrase "with glucose-containing perfusate". As amended, the title matches the preamble of claims 23 and 68 and is believed to be adequately descriptive. Withdrawal of the objection to the title is respectfully requested.

Claim 80 is added herein. Claim 80 recites a method for determining a glucose concentration in a body fluid with glucose-containing perfusate. The method comprises the steps of providing a microdialysis probe, a measuring cell having a sensor, and a control device, inserting the microdialysis probe into the body fluid, passing the perfusate having a pre-determined starting content of glucose through the microdialysis probe to obtain a dialysate, transporting the dialysate to the measuring cell, obtaining with the sensor measurement signals from the dialysate, the dialysate serving as an electrolyte and being used to continuously register a measuring current, which correlates with a glucose content of the dialysate in the measuring cell, and adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, wherein the glucose concentration in the body fluid is determined by either using a momentary content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals. Claims 81-87 depend from claim 80. Support for the new claims is found throughout the specification and claims as originally filed. No new matter is added by virtue of the new claims.

Claims 23-50 and 68-79 are rejected under 35 U.S.C. 112, second paragraph as being indefinite. The rejection is traversed in light of the amendments to claims 23 and 68. Support for the amendments is found in the specification, particularly at page 8 lines

10-18 and page 10 lines 5-21. No new matter is added by virtue of the amendments. The rejection sets forth several points, which will be addressed below.

Regarding claim 23:

1. The rejection proffers that at line 8, "the measuring cell" lacks antecedent basis. The claim has been amended at line 4 to change "a measurement cell" to "a measuring cell". As such, sufficient antecedent basis now exists for "a measuring cell"

2. The rejection proffers that the obtaining measurement signals does not state how the signals are obtained nor from what. The "obtaining" step of the claim has been amended. As such, it is submitted that it is now sufficiently clear from where the signals are obtained "from the dialysate" and how the signals are obtained "with the sensor . . . the dialysate serving as an electrolyte and being used to continuously register a measuring current".

3. The rejection proffers that the next step, "measuring the measurement signals" is not understood. In view of the amendments to the "obtaining" step as discussed above, this step has been removed from the claim.

4. The rejection proffers that there are no steps presented to accomplish the last determining step. The claim has been amended to recite an intermediate step of determining a base line value and the existence of a peak value. It is from these values that the glucose concentration determination is made.

To further clarify this point, the claim has been amended to recite that the glucose concentration in the body fluid is determined by "either using a momentary content of glucose in the perfusate as a measure for the glucose content of the body fluid when a deviation between the peak value and the base line value is negligible or by determining the glucose content of the body fluid directly from the obtained measurement signals". As such, steps have been presented for the determination of glucose concentration.

5. The rejection proffers that there may be some confusion between the terms "content" and "concentration" in the claims. It is submitted that one of ordinary skill in the art is fully aware of the common meaning of each term and specifically that "content" is the amount of the specified substance and that "concentration" is the amount of the specified substance in a unit amount of another substance. Antecedent support is

provided for each of the terms. Therefore, it is submitted that confusion does not exist as to these terms in the claims.

Regarding claims 68-79:

1. The rejection proffers that the phrase "in alternating successive transport and dialysis intervals" is not understood. It is noted that claims 68-79 do not include such a phrase. However, dependent claims 33-36, which depend from claim 23 each include that phrase. Claims 33-36 have been amended accordingly to change the phrase to read "in alternating intervals at different flow rates". The claims as amended are believed to be sufficiently definite.

2. The rejection proffers that "measuring measurement signals" is unclear because no measurement signals have been obtained and what they might be measured for is not seen. In view of the amendments to the "obtaining" step, which are similar to those of claim 23, which has been discussed above, this "measuring" step has been removed from claim 68.

3. The rejection asks "how can one adjust the starting content of glucose if one must first measure the glucose concentration?

The claim has been amended to recite that the starting content of glucose is pre-determined, and thus a known quantity. This pre-determined content is adjusted based upon the measured glucose concentration of the body fluid for future passage of the perfusate through the microdialysis probe.

Claim 68 recites that it is from the measurement signals that the command variable, which corresponds with the glucose concentration of the body fluid, is derived. As such, it is necessary to measure the glucose concentration of the body fluid in order to determine the necessary adjustment of the starting content of the glucose in the perfusate.

4. The rejection asks, "If the starting content of glucose is set according to a command of some sort, how can the momentary starting content of glucose [in the perfusate] be a measure of glucose content of the body fluid?"

As stated above, the starting content of glucose in the perfusate pre-determined, and thus is a known quantity. The momentary content of glucose in the perfusate is used as a measure for the glucose content when a deviation between a measured peak value

and the base line value is negligible. At such times, the starting content of glucose in the perfusate is generally equal to the content of glucose in the body fluid.

5. The rejection states that "If feedback is intended to adjust the starting glucose concentration, it is not found in the claims as presented". Claims 23 and 68 have each been amended to alter the last "determining step" to a wherein clause. Feedback is found within the adjusting steps of claims 23 and 68 to adjust the starting content of glucose in the perfusate. Specifically, feedback may be explained as follows:

1. The perfusate has a starting content of glucose

2. Measurement signals are obtained that correlate with the glucose content of the dialysate (note: one of ordinary skill in the art would readily recognize that the perfusate is entering and the dialysate is leaving the microdialysis probe).

3. The starting content of glucose in the perfusate is adjusted to a value that corresponds to that of the body fluid, which value was derived from the measurement signals - which correlate with the glucose content of the dialysate.

As such, it is submitted that the steps necessary to adjust the starting content of glucose in the perfusate are adequately set forth.

In light of the above amendments, the claims are believed to be sufficiently definite for purposes of 35 U.S.C. 112, second paragraph. Reconsideration of the rejection in light of the amendments, leading to withdrawal of the rejection and allowance of the claims is respectfully requested.

The rejection under 35 U.S.C. 103(a) over U.S. Patent No. 6,091,976 to Pfeiffer et al. was maintained.

The rejection proffers that the "adjusting step" of the claimed invention is so vague as to not be possible to distinguish from Pfeiffer. The claims have been amended to further clarify the invention as discussed above. In light of the amendments, the proffer is respectfully traversed. Unlike Pfeiffer, the idea behind the invention is to adapt the glucose content of the perfusate to the glucose concentration of the body fluid. There is simply no disclosure or suggestion in Pfeifer et al. of adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid, as presently claimed.

As previously stated in the last Reply, the adjusting step of claims 23 and 68 specifically recite, "adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid". This adjustment offsets glucose gradients and hence reduces the period required for a complete dialysis equilibration. The perfusate glucose concentration of Pfeifer et al. is static and is not set, let alone adjusted, based on the tissue glucose concentration. Instead, Pfeiffer et al. teaches that its glucose concentration is simply set within the physiological range, for instance at 5 mmol/ltr. See, Column 4 lines 52-54. As such, there is no disclosure or suggestion in Pfeifer et al. of adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid, as presently claimed.

The only time the glucose concentration of Pfeiffer et al. is altered from the physiological range is during the conduct of signal validation or qualitative comparison measurements. See, Column 5 lines 10-13. These measurements, however, teach away from the presently claimed invention. Specifically, during these validity tests, the glucose concentration in the perfusion solution (30) may be alternatively changed to a sugar-deficiency value and to an excess sugar value to emit a warning signal. See, Column 5 lines 13-16. Neither of these values are derived from the measurement signals of the measuring cell as required by the present claims. Further, the values of Pfeiffer are not determined by either using a momentary content of glucose in the perfusate or by determining the glucose content of the body fluid directly from the obtained measurement signals.

In order to support an obviousness rejection, it is necessary that Pfeiffer et al. provide some teaching, suggestion, or incentive to be modified as proffered by the rejection. Here, it is submitted that only with hindsight, in view of Applicants specification, could one of skill in the art derive from Pfeiffer et al. a suggestion to the invention as it is presently claimed.

It is therefore respectfully submitted that Pfeiffer et al. cannot be said to provide suggestion or motivation to be modified to meet the requirements of amended claim 23, that being a method for determining the glucose concentration in a body fluid with glucose-containing perfusate, wherein the method comprises the steps of "providing a microdialysis probe, a measuring cell having a sensor, and a control device,

inserting the microdialysis probe into the body fluid, passing the perfusate having a pre-determined starting content of glucose through the microdialysis probe to obtain a dialysate, transporting the dialysate to the measuring cell, obtaining with the sensor measurement signals from the dialysate, the dialysate serving as an electrolyte and being used to continuously register as a measuring current, which correlates with a glucose content of the dialysate in the measuring cell, determining from the measurement signals a base line value corresponding to a starting concentration of glucose in the perfusate and the existence of a peak value, the peak value being present when there are differences in concentration between the starting concentration of glucose in the perfusate and the concentration of glucose in the body fluid, and adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, wherein the glucose concentration in the body fluid is determined by either using a momentary content of glucose in the perfusate as a measure for the glucose content of the body fluid when a deviation between the peak value and the base line value is negligible or by determining the glucose content of the body fluid directly from the obtained measurement signals." Claims 24-50 depend from amended claim 23.

Likewise, it is submitted that Pfeiffer et al. cannot be said to provide suggestion or motivation to be modified to meet the requirements of amended claim 68, that being a method for determining the glucose concentration in a body fluid with glucose-containing perfusate, the method comprising the steps of "providing a microdialysis probe, a measuring cell having a sensor, and a control device, inserting the microdialysis probe into the body fluid, passing the perfusate having a pre-determined starting content of glucose through the microdialysis probe at different flow rates to obtain a dialysate, transporting the dialysate to the measuring cell, obtaining with the sensor measurement signals from the dialysate, the dialysate serving as an electrolyte and being used to continuously register as a measuring current, which correlates with a glucose content of the dialysate in the measuring cell, determining from the measurement signals a base line value corresponding to a starting concentration of glucose in the perfusate and the existence of a peak value, the peak value being present when there are differences in

concentration between the starting concentration of glucose in the perfusate and the concentration of glucose in the body fluid, and adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, wherein the glucose concentration in the body fluid is determined by either using a momentary content of glucose in the perfusate as a measure for the glucose content of the body fluid when a deviation between the peak value and the base line value is negligible or by determining the glucose content of the body fluid directly from the obtained measurement signals." Claims 69-79 depend from claim 68.

It is respectfully contended that the differences between the claimed invention and the cited art are such that Applicants' invention as a whole would not have been obvious to one of ordinary skill in the art at the time the invention was made. It is respectfully contended that the claimed invention meets the test of patentability under 35 U.S.C. 103(a). Entry of the amendments leading to reconsideration of the rejection of the claims and withdrawal of the rejection is respectfully requested.

This application is deemed to be in condition for allowance and as such is respectfully requested. In addition, it is requested that this paper be considered as a Petition for an Extension of Time sufficient to effect a timely response and fees be charged to Deposit Account No. 50-0877.

Respectfully submitted,

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Jill L. Woodburn, Reg. No. 39,874
The Law Office of Jill L. Woodburn, L.L.C.
128 Shore Drive
Ogden Dunes, IN
Telephone No.: 219-764-4005
Facsimile No.: 219-764-4070